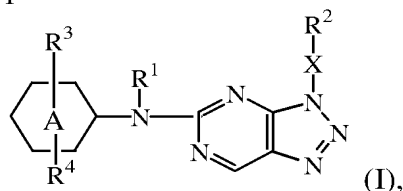


This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

Claims

1. (Currently amended) A compound of formula



a *N*-oxide, a pharmaceutically acceptable addition salt, a quaternary amine and a stereochemically isomeric form thereof, wherein

ring A represents phenyl, ~~pyridyl, pyrimidinyl, pyridazinyl or pyrazinyl~~;

R^1 represents hydrogen; aryl; formyl; C_{1-6} alkylcarbonyl; C_{1-6} alkyl; C_{1-6} alkyloxycarbonyl; C_{1-6} alkyl substituted with formyl, C_{1-6} alkylcarbonyl, C_{1-6} alkyloxycarbonyl, C_{1-6} alkylcarbonyloxy; or C_{1-6} alkyloxy C_{1-6} alkylcarbonyl optionally substituted with C_{1-6} alkyloxycarbonyl;

X represents a direct bond; $-(CH_2)_{n3}-$ or $-(CH_2)_{n4}-X_{1a}-X_{1b}-$;

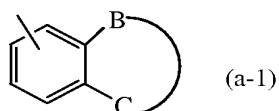
with n_3 representing an integer with value 1, 2, 3 or 4;

with n_4 representing an integer with value 1 or 2;

with X_{1a} representing O, $C(=O)$ or NR^5 ; and

with X_{1b} representing a direct bond or C_{1-2} alkyl;

R^2 represents C_{3-7} cycloalkyl; phenyl; a 4, 5, 6- or 7-membered monocyclic heterocycle containing at least one heteroatom selected from O, S or N; benzoxazolyl or a radical of formula



wherein $-B-C-$ represents a bivalent radical of formula

$-CH_2-CH_2-CH_2-$ (b-1);

$-CH_2-CH_2-CH_2-CH_2-$ (b-2);

$-X_1-CH_2-CH_2-(CH_2)_n-$ (b-3);

$-X_1-CH_2-(CH_2)_n-X_1-$ (b-4);

$-X_1-(CH_2)_n-CH=CH-$ (b-5);

$-CH=N-X_1-$ (b-6);

with X_1 representing O or NR^5 ;

n representing an integer with value 0, 1, 2 or 3;

n' representing an integer with value 0 or 1;

wherein said R² substituent, where possible, may optionally be substituted with at least one substituent selected from halo; hydroxy; C₁₋₆alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C₁₋₄alkyloxy, C₁₋₄alkyloxyC₁₋₄alkyloxy, C₁₋₄alkylcarbonyl, C₁₋₄alkyloxycarbonyl, C₁₋₄alkylcarbonyloxy, NR⁶R⁷, -C(=O)-NR⁶R⁷, -NR⁵-C(=O)-NR⁶R⁷, -S(=O)_{n1}-R⁸ or -NR⁵-S(=O)_{n1}-R⁸; C₂₋₆alkenyl or C₂₋₆alkynyl, each optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C₁₋₄alkyloxy, C₁₋₄alkylcarbonyl, C₁₋₄alkyloxycarbonyl, C₁₋₄alkylcarbonyloxy, NR⁶R⁷, -C(=O)-NR⁶R⁷, -NR⁵-C(=O)-NR⁶R⁷, -S(=O)_{n1}-R⁸ or -NR⁵-S(=O)_{n1}-R⁸; polyhalo-C₁₋₆alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C₁₋₄alkyloxy, C₁₋₄alkyloxyC₁₋₄alkyloxy, C₁₋₄alkylcarbonyl, C₁₋₄alkyloxycarbonyl, C₁₋₄alkylcarbonyloxy, NR⁶R⁷, -C(=O)-NR⁶R⁷, -NR⁵-C(=O)-NR⁶R⁷, -S(=O)_{n1}-R⁸ or -NR⁵-S(=O)_{n1}-R⁸; C₁₋₆alkyloxy optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C₁₋₄alkyloxy, C₁₋₄alkylcarbonyl, C₁₋₄alkyl-oxycarbonyl, C₁₋₄alkylcarbonyloxy, NR⁶R⁷, -C(=O)-NR⁶R⁷, -NR⁵-C(=O)-NR⁶R⁷, -S(=O)_{n1}-R⁸ or -NR⁵-S(=O)_{n1}-R⁸; polyhaloC₁₋₆alkyloxy optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C₁₋₄alkyloxy, C₁₋₄alkyloxyC₁₋₄alkyloxy, C₁₋₄alkylcarbonyl, C₁₋₄alkyloxycarbonyl, C₁₋₄alkylcarbonyloxy, NR⁶R⁷, -C(=O)-NR⁶R⁷, -NR⁵-C(=O)-NR⁶R⁷, -S(=O)_{n1}-R⁸ or -NR⁵-S(=O)_{n1}-R⁸; C₁₋₆alkylthio; polyhaloC₁₋₆alkylthio; C₁₋₆alkyloxycarbonyl; C₁₋₆alkylcarbonyloxy; C₁₋₆alkylcarbonyl; polyhaloC₁₋₆alkylcarbonyl; cyano; carboxyl; NR⁶R⁷; C(=O)NR⁶R⁷; -NR⁵-C(=O)-NR⁶R⁷; -NR⁵-C(=O)-R⁵; -S(=O)_{n1}-R⁸; -NR⁵-S(=O)_{n1}-R⁸; -S-CN; -NR⁵-CN; aryloxy; arylthio; arylcarbonyl; arylC₁₋₄alkyl; arylC₁₋₄alkyloxy; a 5-or 6-membered monocyclic heterocycle containing at least one heteroatom selected from O, S or N and said 5-or 6-membered monocyclic heterocycle optionally being substituted with at least

one substituent selected from R⁹; or $-(CH_2)_{n2}-X_2-(CH_2)_{n2}-N \begin{array}{c} \diagup \diagdown \\ \diagdown \diagup \end{array} \begin{array}{c} X_3 \\ X_3 \end{array}$;

with n₂ representing an integer with value 0, 1, 2, 3 or 4;

with X₂ representing O, NR⁵ or a direct bond;

with X₃ representing O, CH₂, CHOH, CH-N(R⁵)₂, NR⁵ or N-C(=O)-C₁₋₄alkyl;

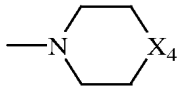
R^3 represents halo; hydroxy; C_{1-6} alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C_{1-4} alkyloxy, C_{1-4} alkyloxy- C_{1-4} alkyloxy, C_{1-4} alkylcarbonyl, C_{1-4} alkyloxycarbonyl, C_{1-4} alkylcarbonyloxy, $NR^{6b}R^{7b}$, $-C(=O)-NR^{6b}R^{7b}$, $-NR^5-C(=O)-NR^{6b}R^{7b}$, $-S(=O)_{n1}-R^{8a}$ or $-NR^5-S(=O)_{n1}-R^{8a}$; C_{2-6} alkenyl or C_{2-6} alkynyl, each optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C_{1-4} alkyloxy, C_{1-4} alkylcarbonyl, C_{1-4} alkyloxycarbonyl, C_{1-4} alkylcarbonyloxy, $NR^{6b}R^{7b}$, $-C(=O)-NR^{6b}R^{7b}$, $-NR^5-C(=O)-NR^{6b}R^{7b}$, $-S(=O)_{n1}-R^{8a}$ or $-NR^5-S(=O)_{n1}-R^{8a}$; polyhalo C_{1-6} alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C_{1-4} alkyloxy, C_{1-4} alkyloxy- C_{1-4} alkyloxy, C_{1-4} alkylcarbonyl, C_{1-4} alkyloxycarbonyl, C_{1-4} alkylcarbonyloxy, $NR^{6b}R^{7b}$, $-C(=O)-NR^{6b}R^{7b}$, $-NR^5-C(=O)-NR^{6b}R^{7b}$, $-S(=O)_{n1}-R^{8a}$ or $-NR^5-S(=O)_{n1}-R^{8a}$; C_{1-6} alkyloxy optionally substituted with one substituent selected from hydroxy, cyano, carboxyl, C_{1-4} alkyloxy, C_{1-4} alkylcarbonyl, C_{1-4} alkyloxy-carbonyl, C_{1-4} alkylcarbonyloxy, $NR^{6b}R^{7b}$, $-C(=O)-NR^{6b}R^{7b}$, $-NR^5-C(=O)-NR^{6b}R^{7b}$, $-S(=O)_{n1}-R^{8a}$ or $-NR^5-S(=O)_{n1}-R^{8a}$; polyhalo C_{1-6} alkyloxy optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C_{1-4} alkyloxy, C_{1-4} alkyloxy C_{1-4} alkyloxy, C_{1-4} alkylcarbonyl, C_{1-4} alkyloxycarbonyl, C_{1-4} alkylcarbonyloxy, $NR^{6b}R^{7b}$, $-C(=O)-NR^{6b}R^{7b}$, $-NR^5-C(=O)-NR^{6b}R^{7b}$, $-S(=O)_{n1}-R^{8a}$ or $-NR^5-S(=O)_{n1}-R^{8a}$; C_{1-6} alkylthio; polyhalo C_{1-6} alkylthio; C_{1-6} alkyloxycarbonyl; C_{1-6} alkylcarbonyloxy; C_{1-6} alkylcarbonyl; polyhalo- C_{1-6} alkylcarbonyl; cyano; carboxyl; aryloxy; arylthio; arylcarbonyl; $NR^{6b}R^{7b}$; $C(=O)-NR^{6b}R^{7b}$; $-NR^5-C(=O)-NR^{6b}R^{7b}$; $-NR^5-C(=O)-R^5$; $-S(=O)_{n1}-R^{8a}$; $-NR^5-S(=O)_{n1}-R^{8a}$; $-S-CN$; or $-NR^5-CN$;

R^4 represents hydrogen; halo; hydroxy; C_{1-4} alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C_{1-4} alkyloxy, C_{1-4} alkylcarbonyl, C_{1-4} alkyloxycarbonyl, C_{1-4} alkylcarbonyloxy, $NR^{10}R^{11}$, $-C(=O)-NR^{10}R^{11}$, $-NR^5-C(=O)-NR^{10}R^{11}$, $-S(=O)_{n1}-R^{12}$ or $-NR^5-S(=O)_{n1}-R^{12}$; C_{2-4} alkenyl or C_{2-4} alkynyl, each optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C_{1-4} alkyloxy, C_{1-4} alkylcarbonyl, C_{1-4} alkyloxycarbonyl, C_{1-4} alkylcarbonyloxy, $NR^{10}R^{11}$, $-C(=O)-NR^{10}R^{11}$, $-NR^5-C(=O)-NR^{10}R^{11}$, $-S(=O)_{n1}-R^{12}$ or $-NR^5-S(=O)_{n1}-R^{12}$; polyhalo C_{1-3} alkyl; C_{1-4} alkyloxy optionally substituted with carboxyl; polyhalo C_{1-3} alkyloxy; C_{1-4} alkylthio; polyhalo C_{1-3} alkylthio; C_{1-4} alkyloxycarbonyl; C_{1-4} alkylcarbonyloxy; C_{1-4} alkylcarbonyl; polyhalo C_{1-4} alkylcarbonyl; nitro; cyano; carboxyl; $NR^{10}R^{11}$;

$C(=O)NR^{10}R^{11}$; $-NR^5-C(=O)-NR^{10}R^{11}$; $-NR^5-C(=O)-R^5$; $-S(=O)_{n1}-R^{12}$;
 $-NR^5-S(=O)_{n1}-R^{12}$; $-S-CN$; or $-NR^5-CN$;

R^5 represents hydrogen; C_{1-4} alkyl or C_{2-4} alkenyl;

R^6 and R^7 each independently represent hydrogen; cyano; C_{1-6} alkylcarbonyl optionally substituted with C_{1-4} alkyloxy or carboxyl; C_{1-6} alkyloxycarbonyl; C_{3-7} cycloalkylcarbonyl; adamantanylcabonyl; C_{1-4} alkyloxy C_{1-4} alkyl; C_{1-4} alkyl substituted with C_{1-4} alkyl- NR^5 -; C_{1-6} alkyl optionally substituted with at least one substituent selected from halo, hydroxy, cyano, carboxyl, C_{1-4} alkyloxy, polyhalo-

C_{1-4} alkyl, C_{1-4} alkyloxy C_{1-4} alkyloxy, $NR^{6a}R^{7a}$, $C(=O)NR^{6a}R^{7a}$ or ; with X_4 representing O, CH_2 , $CHOH$, $CH-N(R^5)_2$, NR^5 or $N-C(=O)-C_{1-4}$ alkyl;

R^{6a} and R^{7a} each independently represent hydrogen; C_{1-4} alkyl; C_{1-4} alkylcarbonyl or a 5- or 6-membered monocyclic heterocycle containing at least one heteroatom selected from O, S or N;

R^{6b} and R^{7b} each independently represent hydrogen; cyano; C_{1-6} alkylcarbonyl optionally substituted with C_{1-4} alkyloxy or carboxyl; C_{1-6} alkyloxycarbonyl; C_{3-7} cycloalkylcarbonyl; adamantanylcabonyl; C_{1-4} alkyloxy C_{1-4} alkyl; C_{1-4} alkyl substituted with C_{1-4} alkyl- NR^5 -; C_{1-6} alkyl optionally substituted with at least one substituent selected from halo, hydroxy, cyano, carboxyl, C_{1-4} alkyloxy, polyhalo C_{1-4} alkyl, C_{1-4} alkyloxy- C_{1-4} alkyloxy, $NR^{6c}R^{7c}$ or $C(=O)NR^{6c}R^{7c}$;

R^{6c} and R^{7c} each independently represent hydrogen; C_{1-4} alkyl or C_{1-4} alkylcarbonyl;

R^8 represents C_{1-4} alkyl optionally substituted with hydroxy; polyhalo C_{1-4} alkyl or NR^6R^7 ;

R^{8a} represents C_{1-4} alkyl optionally substituted with hydroxy; polyhalo C_{1-4} alkyl or $NR^{6b}R^{7b}$;

R^9 represents halo; hydroxy; C_{1-6} alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C_{1-4} alkyloxy, C_{1-4} alkylcarbonyl, C_{1-4} alkyloxycarbonyl, C_{1-4} alkylcarbonyloxy, NR^6R^7 , $-C(=O)-NR^6R^7$, $-NR^5-C(=O)-NR^6R^7$, $-S(=O)_{n1}-R^8$ or $-NR^5-S(=O)_{n1}-R^8$; C_{2-6} alkenyl or C_{2-6} alkynyl, each optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C_{1-4} alkyloxy, C_{1-4} alkylcarbonyl, C_{1-4} alkyloxycarbonyl, C_{1-4} alkylcarbonyloxy, NR^6R^7 , $-C(=O)-NR^6R^7$, $-NR^5-C(=O)-NR^6R^7$, $-S(=O)_{n1}-R^8$ or $-NR^5-S(=O)_{n1}-R^8$; polyhalo C_{1-6} alkyl; C_{1-6} alkyloxy optionally substituted with carboxyl; polyhalo C_{1-6} alkyloxy; C_{1-6} alkylthio; polyhalo C_{1-6} alkylthio; C_{1-6} alkyloxycarbonyl; C_{1-6} alkylcarbonyloxy; C_{1-6} alkylcarbonyl; cyano; carboxyl; NR^6R^7 ; $C(=O)NR^6R^7$; $-NR^5-C(=O)-NR^6R^7$; $-NR^5-C(=O)-R^5$; $-S(=O)_{n1}-R^8$; $-NR^5-S(=O)_{n1}-R^8$; $-S-CN$; or $-NR^5-CN$;

R^{10} and R^{11} each independently represent hydrogen; C_{1-6} alkyl; cyano;
 C_{1-6} alkylcarbonyl; C_{1-4} alkyloxy C_{1-4} alkyl; or C_{1-4} alkyl substituted with
 C_{1-4} alkyl- NR^5 -;

R^{12} represents C_{1-4} alkyl or $NR^{10}R^{11}$;

n_1 represents an integer with value 1 or 2;

aryl represents phenyl or phenyl substituted with at least one substituent selected from halo,
 C_{1-6} alkyl, C_{3-7} cycloalkyl, C_{1-6} alkyloxy, cyano, nitro, polyhalo C_{1-6} alkyl or polyhalo C_{1-6} alkyloxy.

2. (Original) A compound according to claim 1 wherein

X represents a direct bond; $-(CH_2)_{n_3}$ - or $-(CH_2)_{n_4}-X_a-X_b$;

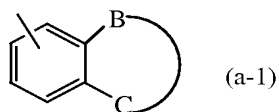
with n_3 representing an integer with value 1, 2, 3 or 4;

with n_4 representing an integer with value 1 or 2;

with X_a representing O or NR^5 ; and

with X_b representing a direct bond or C_{1-2} alkyl;

R^2 represents C_{3-7} cycloalkyl; phenyl or a 4, 5, 6- or 7-membered monocyclic heterocycle
containing at least one heteroatom selected from O, S or N; or a radical of formula



wherein $-B-C-$ represents a bivalent radical of formula

$-CH_2-CH_2-CH_2-$ (b-1);

$-CH_2-CH_2-CH_2-CH_2-$ (b-2);

$-X_1-CH_2-CH_2-(CH_2)_n-$ (b-3);

$-X_1-CH_2-(CH_2)_n-X_1-$ (b-4);

$-X_1-(CH_2)_{n'}-CH=CH-$ (b-5);

with X_1 representing O or NR^5 ;

n representing an integer with value 0, 1, 2 or 3;

n' representing an integer with value 0 or 1;

wherein said R^2 substituent, where possible, may optionally be substituted with at least one
substituent selected from halo; hydroxy; C_{1-6} alkyl optionally substituted with at least one
substituent selected from hydroxy, cyano, carboxyl, C_{1-4} alkyloxy, C_{1-4} alkylcarbonyl, C_{1-4}
alkyloxycarbonyl, C_{1-4} alkylcarbonyloxy, NR^6R^7 ,
 $-C(=O)-NR^6R^7$, $-NR^5-C(=O)-NR^6R^7$, $-S(=O)_{n_1}-R^8$ or $-NR^5-S(=O)_{n_1}-R^8$; C_{2-6} alkenyl or
 C_{2-6} alkynyl, each optionally substituted with at least one substituent selected from

hydroxy, cyano, carboxyl, C₁₋₄alkyloxy, C₁₋₄alkylcarbonyl, C₁₋₄alkyloxycarbonyl, C₁₋₄alkylcarbonyloxy, NR⁶R⁷, -C(=O)-NR⁶R⁷, -NR⁵-C(=O)-NR⁶R⁷, -S(=O)_{n1}-R⁸ or -NR⁵-S(=O)_{n1}-R⁸; polyhaloC₁₋₆alkyl; C₁₋₆alkyloxy optionally substituted with carboxyl; polyhaloC₁₋₆alkyloxy; C₁₋₆alkylthio; polyhaloC₁₋₆alkylthio; C₁₋₆alkyloxycarbonyl; C₁₋₆alkylcarbonyloxy; C₁₋₆alkylcarbonyl; polyhaloC₁₋₆alkylcarbonyl; cyano; carboxyl; NR⁶R⁷; C(=O)NR⁶R⁷; -NR⁵-C(=O)-NR⁶R⁷; -NR⁵-C(=O)-R⁵; -S(=O)_{n1}-R⁸; -NR⁵-S(=O)_{n1}-R⁸; -S-CN; -NR⁵-CN; aryloxy; arylthio; arylcarbonyl; arylC₁₋₄alkyl; arylC₁₋₄alkyloxy; a 5-or 6-membered monocyclic heterocycle containing at least one heteroatom selected from O, S or N and said 5-or 6-membered monocyclic heterocycle optionally being substituted

with at least one substituent selected from R⁹; or $-(CH_2)_{n2}-X_2-(CH_2)_{n2}-N \begin{array}{c} \diagup \\ \diagdown \end{array} \begin{array}{c} \diagdown \\ \diagup \end{array} X_3$;

with n₂ representing an integer with value 0, 1, 2, 3 or 4;

with X₂ representing O, NR⁵ or a direct bond;

with X₃ representing O or NR⁵;

R³ represents halo; hydroxy; C₁₋₆alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C₁₋₄alkyloxy, C₁₋₄alkylcarbonyl, C₁₋₄alkyloxycarbonyl, C₁₋₄alkylcarbonyloxy, NR^{6b}R^{7b}, -C(=O)-NR^{6b}R^{7b}, -NR⁵-C(=O)-NR^{6b}R^{7b}, -S(=O)_{n1}-R^{8a} or -NR⁵-S(=O)_{n1}-R^{8a}; C₂₋₆alkenyl or C₂₋₆alkynyl, each optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C₁₋₄alkyloxy, C₁₋₄alkylcarbonyl, C₁₋₄alkyloxycarbonyl, C₁₋₄alkylcarbonyloxy, NR^{6b}R^{7b}, -C(=O)-NR^{6b}R^{7b}, -NR⁵-C(=O)-NR^{6b}R^{7b}, -S(=O)_{n1}-R^{8a} or -NR⁵-S(=O)_{n1}-R^{8a}; polyhaloC₁₋₆alkyl; C₁₋₆alkyloxy optionally substituted with carboxyl; polyhaloC₁₋₆alkyloxy; C₁₋₆alkylthio; polyhaloC₁₋₆alkylthio; C₁₋₆alkyloxycarbonyl; C₁₋₆alkylcarbonyloxy; C₁₋₆alkylcarbonyl; polyhaloC₁₋₆alkylcarbonyl; nitro; cyano; carboxyl; NR^{6b}R^{7b}; C(=O)NR^{6b}R^{7b}; -NR⁵-C(=O)-NR^{6b}R^{7b}; -NR⁵-C(=O)-R⁵; -S(=O)_{n1}-R^{8a}; -NR⁵-S(=O)_{n1}-R^{8a}; -S-CN; or -NR⁵-CN;

R⁵ represents hydrogen or C₁₋₄alkyl;

R⁶ and R⁷ each independently represent hydrogen; cyano; C₁₋₆alkylcarbonyl;

C₁₋₄alkyloxyC₁₋₄alkyl; C₁₋₄alkyl substituted with C₁₋₄alkyl-NR⁵-; C₁₋₆alkyl optionally substituted with hydroxy, C₁₋₄alkyloxy, C₁₋₄alkyloxyC₁₋₄alkyloxy, NR^{6a}R^{7a}, C(=O)NR^{6a}R^{7a}

or $\begin{array}{c} \diagup \\ \diagdown \end{array} N \begin{array}{c} \diagdown \\ \diagup \end{array} X_4$; with X₄ representing O or NR⁵;

R^{6a} and R^{7a} each independently represent hydrogen; C_{1-4} alkyl; C_{1-4} alkylcarbonyl or a 5- or 6-membered monocyclic heterocycle containing at least one heteroatom selected from O, S or N;

R^{6b} and R^{7b} each independently represent hydrogen; cyano; C_{1-6} alkylcarbonyl; C_{1-4} alkyloxy C_{1-4} alkyl; C_{1-4} alkyl substituted with C_{1-4} alkyl- NR^5 ; C_{1-6} alkyl optionally substituted with hydroxy, C_{1-4} alkyloxy, C_{1-4} alkyloxy C_{1-4} alkyloxy, $NR^{6a}R^{7a}$ or $C(=O)NR^{6a}R^{7a}$;

R^8 represents C_{1-4} alkyl, polyhalo C_{1-4} alkyl or NR^6R^7 ;

R^{8a} represents C_{1-4} alkyl, polyhalo C_{1-4} alkyl or $NR^{6b}R^{7b}$.

3. (Currently amended) A compound as claimed in claim 1 wherein ~~ring A represents phenyl or pyridyl~~; R^1 represents hydrogen; X represents a direct bond or $-(CH_2)_{n3}$; R^2 represents phenyl or a radical of formula (b-4), wherein said R^2 may optionally be substituted with at least one substituent, in particular 1, 2 or 3 substituents, selected from halo; C_{1-6} alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, NR^6R^7 , $C(=O)NR^6R^7$, C_{1-4} alkyloxy or C_{1-4} alkyloxy C_{1-4} alkyloxy; C_{1-6} alkyloxy; C_{1-6} alkyloxycarbonyl; C_{1-4} alkyloxy C_{1-6} alkyloxy; cyano; carboxyl; $C(=O)NR^6R^7$; $-S(=O)_{n1}-R^8$; aryl C_{1-4} alkyloxy; or a 5- or 6-membered heterocycle containing at least one heteroatom selected from O, S or N and said 5- or 6-membered heterocycle optionally being substituted with at least one substituent selected from R^9 ; R^3 represents halo; hydroxy; C_{1-6} alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C_{1-4} alkyloxy, $NR^{6b}R^{7b}$ or $C(=O)NR^{6b}R^{7b}$; C_{2-6} alkenyl optionally substituted with at least one substituent selected from carboxyl or C_{1-4} alkyl-oxycarbonyl; polyhalo C_{1-6} alkyloxy; C_{1-6} alkyloxy optionally substituted with C_{1-4} alkyloxy; C_{1-6} alkylthio; C_{1-6} alkyloxycarbonyl; C_{1-6} alkylcarbonyl; cyano; carboxyl; $NR^{6b}R^{7b}$; $C(=O)NR^{6b}R^{7b}$; $-NR^5-C(=O)-R^5$; $-S(=O)_{n1}-R^8$; $-NR^5-S(=O)_{n1}-R^8$; or $-S-CN$; R^4 represents hydrogen; halo; C_{1-6} alkyl; cyano; hydroxy; C_{1-6} alkyloxycarbonyl; C_{1-6} alkyloxy; carboxyl; or NR^6R^7 .

4. (Currently amended) A compound as claimed in claim 1 wherein ~~ring A represents phenyl or pyridyl~~; R^1 represents hydrogen; X represents a direct bond; R^2 represents phenyl wherein said R^2 may optionally be substituted with at least one substituent, in particular 1, 2 or 3 substituents, selected from halo; C_{1-6} alkyl substituted with one substituent selected from hydroxy, cyano, NR^6R^7 , $C(=O)NR^6R^7$, C_{1-4} alkyloxy or C_{1-4} alkyloxy C_{1-4} alkyloxy; C_{1-6} alkyloxy; C_{1-6} alkyloxycarbonyl; C_{1-4} alkyloxy C_{1-6} alkyloxy; $C(=O)NR^6R^7$;

-S(=O)_{n1}-R⁸; or a 5-or 6-membered heterocycle containing at least one heteroatom selected from O, S or N and said 5-or 6-membered heterocycle optionally being substituted with at least one substituent selected from R⁹; R³ represents halo; hydroxy; C₁₋₆alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C₁₋₄alkyloxy, NR^{6b}R^{7b} or C(=O)NR^{6b}R^{7b}; C₂₋₆alkenyl optionally substituted with at least one substituent selected from carboxyl or C₁₋₄alkyloxycarbonyl; polyhaloC₁₋₆alkyloxy; C₁₋₆alkyloxy optionally substituted with C₁₋₄alkyloxy or NR^{6b}R^{7b}; C₁₋₆alkylthio; C₁₋₆alkyloxycarbonyl; C₁₋₆alkylcarbonyl; cyano; carboxyl; NR^{6b}R^{7b}; C(=O)NR^{6b}R^{7b}; -S(=O)_{n1}-R⁸; -NR⁵-C(=O)-R⁵; or -NR⁵-S(=O)_{n1}-R⁸; R⁴ represents hydrogen; halo; C₁₋₆alkyl; hydroxy; C₁₋₆alkyloxycarbonyl; C₁₋₆alkyloxy; carboxyl; or NR⁶R⁷.

5. (Previously presented) A compound as claimed in claim 1 wherein the R³ substituent is linked to ring A in meta position compared to the NR¹ linker.

6. (Previously presented) A compound as claimed in claim 1 wherein the R³ substituent is linked to ring A in para position compared to the NR¹ linker.

7. (Previously presented) A compound as claimed in claim 1 wherein R³ represents NR^{6b}R^{7b}.

8. (Previously presented) A compound as claimed in claim 1 wherein X represents a direct bond.

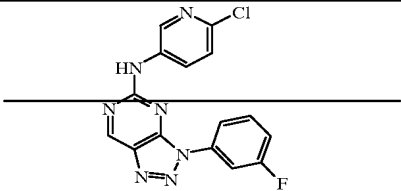
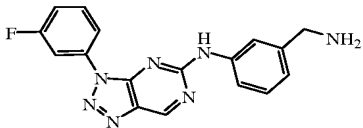
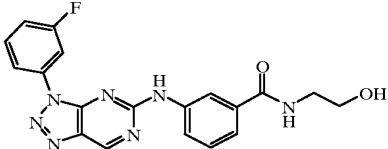
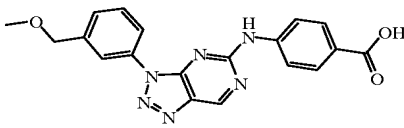
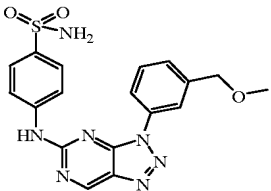
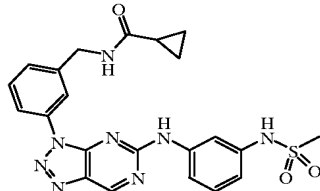
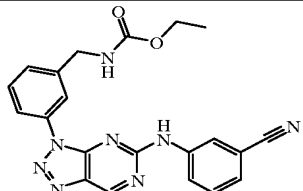
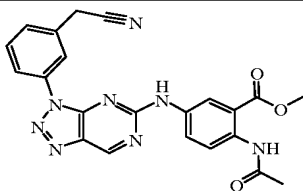
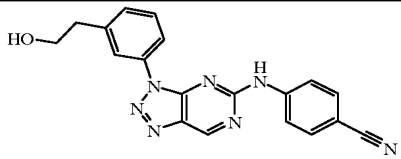
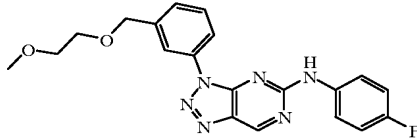
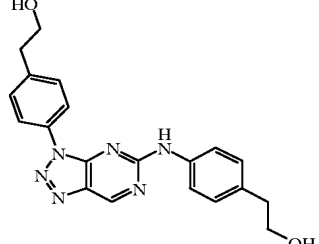
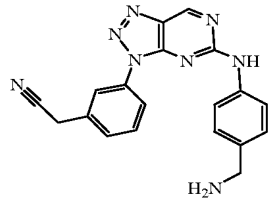
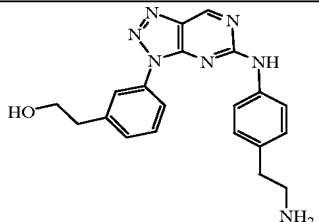
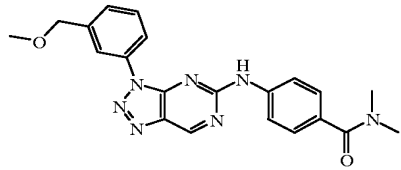
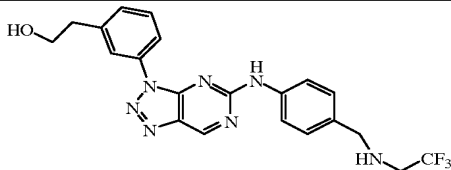
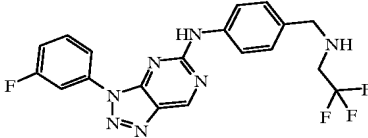
9. (Previously presented) A compound as claimed in claim 1 wherein R² represents C₃₋₇cycloalkyl; phenyl; a 4, 5, 6- or 7-membered monocyclic heterocycle containing at least one heteroatom selected from O, S or N; benzoxazolyl or a radical of formula (a-1) wherein said R² substituent is substituted with at least one substituent selected from C₁₋₆alkyl substituted with NR⁶R⁷; C₂₋₆alkenyl or C₂₋₆alkynyl, each substituted with NR⁶R⁷; polyhaloC₁₋₆alkyl substituted with NR⁶R⁷; C₁₋₆alkyloxy substituted with NR⁶R⁷; polyhaloC₁₋₆alkyloxy substituted with NR⁶R⁷; or NR⁶R⁷.

10. (Previously presented) A compound as claimed in claim 1 wherein R³ represents C₁₋₆alkyl substituted with NR^{6b}R^{7b}; C₂₋₆alkenyl or C₂₋₆alkynyl, each substituted with NR^{6b}R^{7b};

polyhaloC₁₋₆alkyl substituted with NR^{6b}R^{7b}; C₁₋₆alkyloxy substituted with NR^{6b}R^{7b};
polyhaloC₁₋₆alkyloxy substituted with NR^{6b}R^{7b}; or NR^{6b}R^{7b}.

11. (Previously presented) A compound as claimed in claim 1 wherein R² represents C₃₋₇cycloalkyl; phenyl; a 4, 5, 6- or 7-membered monocyclic heterocycle containing at least one heteroatom selected from O, S or N; benzoxazolyl or a radical of formula (a-1), wherein said R² substituent is substituted with at least one substituent selected from halo; polyhaloC₁₋₆alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C₁₋₄alkyloxy, C₁₋₄alkyloxy-, C₁₋₄alkyloxy, C₁₋₄alkylcarbonyl, C₁₋₄alkyloxycarbonyl, C₁₋₄alkylcarbonyloxy, NR⁶R⁷, -C(=O)-NR⁶R⁷, -NR⁵-C(=O)-NR⁶R⁷, -S(=O)_{n1}-R⁸ or -NR⁵-S(=O)_{n1}-R⁸; polyhalo-C₁₋₆alkyloxy optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C₁₋₄alkyloxy, C₁₋₄alkyloxyC₁₋₄alkyloxy, C₁₋₄alkylcarbonyl, C₁₋₄alkyloxycarbonyl, C₁₋₄alkylcarbonyloxy, NR⁶R⁷, -C(=O)-NR⁶R⁷, -NR⁵-C(=O)-NR⁶R⁷, -S(=O)_{n1}-R⁸ or -NR⁵-S(=O)_{n1}-R⁸.

12. (Currently amended) A compound as claimed in claim 1 wherein the compound is selected from the group consisting of

--	--

a *N*-oxide, a pharmaceutically acceptable addition salt, a quaternary amine and a stereochemically isomeric form thereof.

13. (Previously presented) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the compound of claim 1.

14. (Previously presented) A method for the prevention or the treatment of a disease mediated through GSK3 comprising administering a therapeutically effective amount of a compound of claim 1 to a patient in need of treatment for a disease mediated through GSK3.

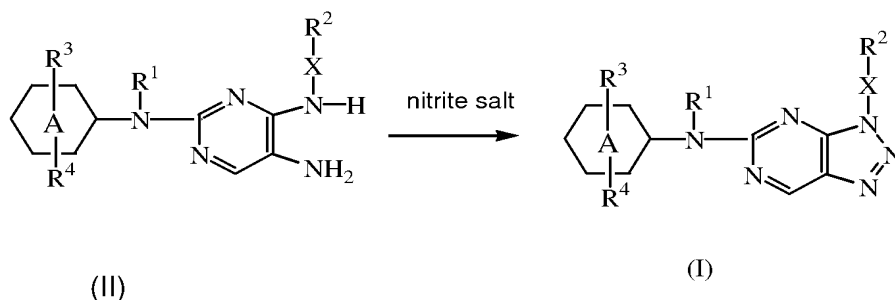
15. (Previously presented) The method for the prevention or the treatment of a disease mediated through GSK3 of claim 14 wherein the disease is selected from the group consisting of bipolar disorder (in particular manic depression), diabetes, Alzheimer's disease, leukopenia, FTDP-17 (Fronto-temporal dementia associated with Parkinson's disease), cortico-basal degeneration, progressive supranuclear palsy, multiple system atrophy, Pick's disease, Niemann Pick's disease type C, Dementia Pugilistica, dementia with tangles only, dementia with tangles and calcification, Downs syndrome, myotonic dystrophy, Parkinsonism-dementia complex of Guam, aids related dementia, Postencephalic Parkinsonism, prion diseases with tangles, subacute sclerosing panencephalitis, frontal lobe degeneration (FLD), argyrophilic grains disease, subacute sclerotizing panencephalitis (SSPE) (late complication of viral infections in the central nervous system), inflammatory diseases, depression, cancer, dermatological disorders, neuroprotection, schizophrenia, and pain.

16. (Previously presented) The method for the prevention or the treatment of a disease mediated through GSK3 of claim 14 wherein the disease is selected from the group consisting of Alzheimer's disease; diabetes; cancer; inflammatory diseases; bipolar disorder; depression; and pain.

17. (Previously presented) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and as active ingredient a therapeutically effective amount of a compound as claimed in claim 1.

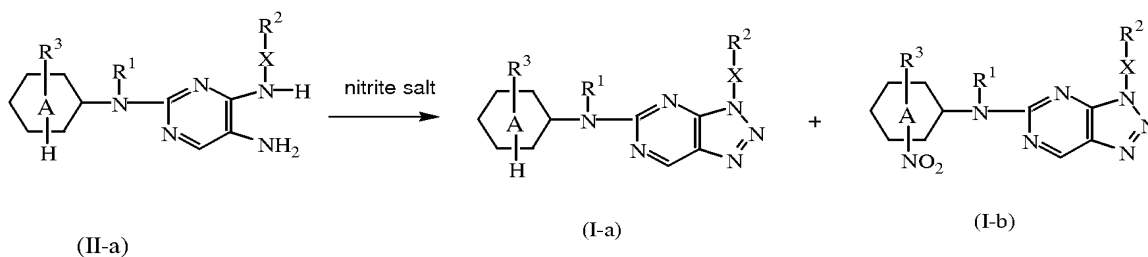
18. (Currently amended) A process for preparing a pharmaceutical composition ~~as claimed in claim 17 characterized in that~~ comprising intimately mixing a therapeutically effective amount of a compound as claimed in claim 1 ~~is intimately mixed~~ with a pharmaceutically acceptable carrier.

19. (Currently amended) A process for preparing a compound as claimed in claim 1, ~~characterized by comprising~~
 a) ~~by~~ cyclizing an intermediate of formula (II) in the presence of a nitrite salt, a suitable solvent, and a suitable acid,



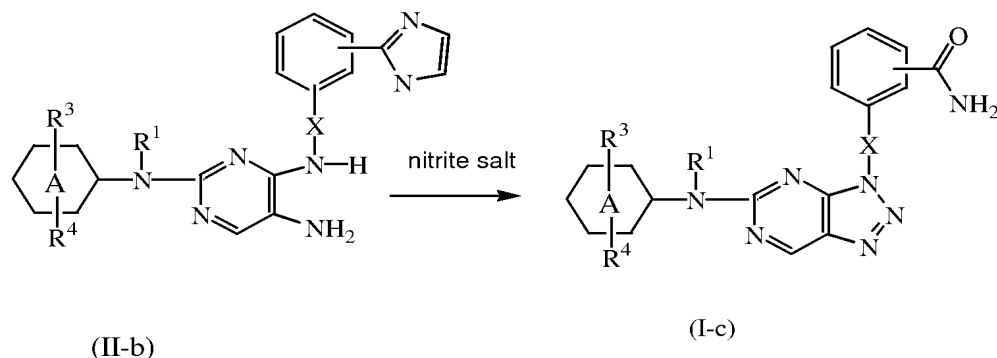
wherein ring A, R^1 to R^4 and X are as defined in claim 1;

b) cyclizing an intermediate of formula (II-a) in the presence of a nitrite salt, a suitable solvent, and a suitable acid,



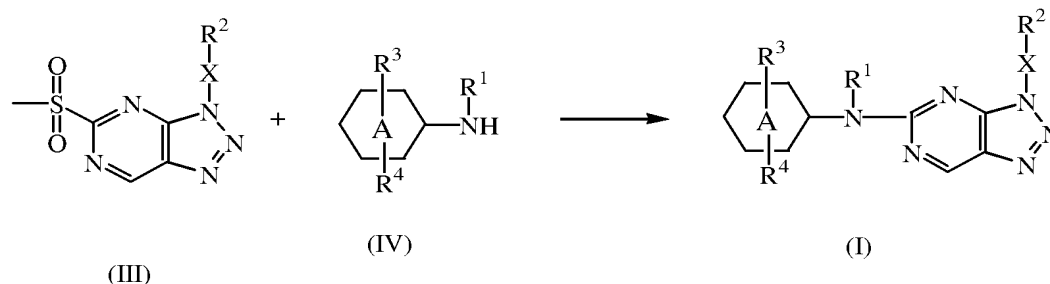
wherein ring A, R^1 to R^3 and X are as defined in claim 1;

c) cyclizing an intermediate of formula (II-b) in the presence of a nitrite salt, a suitable solvent, and a suitable acid,



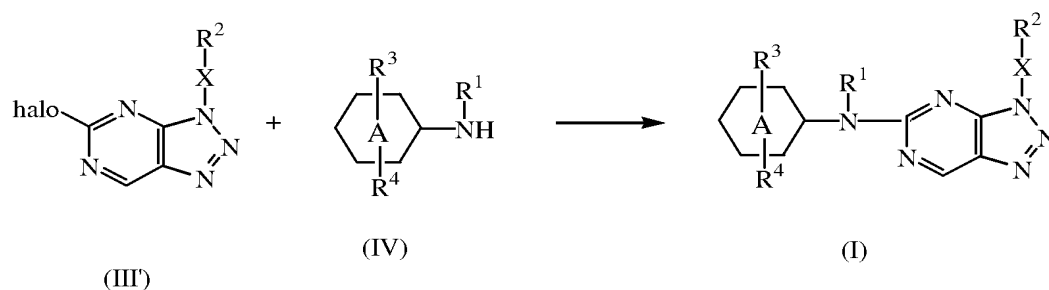
wherein ring A, R^1 , R^3 , R^4 and X are as defined in claim 1;

d) reacting an intermediate of formula (III) with an intermediate of formula (IV) in the presence of a suitable solvent,



wherein ring A, R^1 to R^4 and X are as defined in claim 1;

e) reacting an intermediate of formula (III') with an intermediate of formula (IV) in the presence of a suitable solvent, and optionally in the presence of a suitable base,



or, ~~if desired~~ optionally, converting compounds of formula (I) into each other following art-known transformations, and further, if desired, converting the compounds of formula (I), into a therapeutically active non-toxic acid addition salt by treatment with an acid, or into a therapeutically active non-toxic base addition salt by treatment with a base, or conversely, converting the acid addition salt form into the free base by treatment with alkali, or

DOCKET NO.: JANS-0090 (PRD2066USPCT1)

PATENT

Application No.: 10/564,844

Office Action Dated: May 7, 2007

converting the base addition salt into the free acid by treatment with acid; and, if
~~desired~~optionally, preparing stereochemically isomeric forms, quaternary amines or *N*-oxide
forms thereof.